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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/684,796	10/14/2003	Jonathan David Garman	AVC72	4233

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EXAMINER	
HOWARD, ZACHARY C	

ART UNIT	PAPER NUMBER
1646	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/684,796	GARMAN ET AL.	
	Examiner	Art Unit	
	Zachary C. Howard	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) *5-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-12* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/11/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-4, in the reply filed on 4/25/06 is acknowledged.

Claims 5-12 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made without traverse in the reply filed on 4/25/06.

Claims 1-4 are under consideration.

Specification

The disclosure is objected to because of the following informalities:

(1) Page 96, lines 9-10 of the 5/4/05 substitute specification states:

> "Tables 8A, 8B and 8C show the results of G assay testing (described supra) between the three alpha 2 adrenergic subunits and a subset of PDZ domain. All tests are performed at 10uM concentration of peptide, and the peptide sequence is displayed in column 2."

However, the statement "the peptide sequence is displayed in column 2" is objected to because neither of Table 8A (starting on page 96), Table 8B (starting on page 102) or Table 8C (starting on page 110) displays a peptide sequence in "column 2" (or even a reference SEQ ID NO:). Instead, the second column ("column 2") of each table is titled "Domain". It is noted that the specification as originally filed did include peptide sequences as "column 2" of said Tables; however, in 5/4/2005 substitute specification these three sequences were moved to line 4-6 of page 96.

Claim Rejections - 35 USC § 101, utility

The following is a quotation of 35 U.S.C. § 101:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-4 are rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

Claim 1 is directed to a method of detecting PDZ binding to an alpha adrenergic receptor comprising combining a labeled polypeptide containing an alpha adrenergic receptor C-terminal PL sequence with a PDZ polypeptide and detecting binding between said PL and said PDZ sequence. Claims 2-4 depend from claim 1 and respectively limit the PL polypeptide to a biotinylated peptide (claim 2); a fluorescence labeled peptide (claim 3); or a epitope tagged protein expressed in a host cell (claim 4).

The specification teaches that, "the invention provides methods of modulating localization or function of receptors that bind heteromeric G proteins by antagonizing or promoting binding between a PDZ domain containing protein that binds a PDZ domain" (pg 1). The specification teaches that "blocking interactions between alpha adrenergic receptors and PDZ domains can modulate the effect of signaling through these receptors and provide a new set of therapeutic targets for treatment of diseases or disease stemming from misfunctioning biological processes such as those listed in Table 9" (pg 118). As such, it appears that the asserted utility for the claimed invention is to determine the binding between alpha adrenergic receptors and PDZ proteins, such that the binding can be modulated for therapeutic purposes.

A substantial utility is a practical use which amounts to more than a starting point for further research and investigation and does not require or constitute carrying out further research to identify or reasonably confirm what the practical use might ultimately be. Basic research, such as studying the properties of the claimed product or the mechanisms in which the product is involved, does not constitute a substantial utility.

In the instant case, the asserted utility is not a specific and substantial utility because there is no reasonable correlation between the ability of a particular PDZ protein to bind to an alpha-adrenergic receptor and the ability to modulate the activity of the receptor by altering said binding. The specification in Tables 8A-C provides a long list of PDZ proteins that each have some degree of binding to a small fragment of an alpha-adrenergic receptor sequence in an *in vitro* binding assay. However, the ability to bind to a small fragment of a receptor sequence *in vitro* does not indicate whether or not modification of said binding will actual modify the activity of the receptor protein either *in vitro* or *in vivo*. Binding assays frequently identify protein-protein interactions that have no physiological significance. For example, the relevant art questions the physiological significance of binding between a C-terminal peptide of human α1A-adrenergic receptor and the PDZ domain of neuronal nitric oxide synthase (nNOS). Schepens et al (1997) demonstrated (using a yeast two-hybrid assay) that a protein consisting of the last 114 amino acids of the rat α1C (later renamed α1A) adrenergic receptor was able to bind to the PDZ domain of neuronal nitric oxide synthesis (nNOS; Schepens et al, 1997. FEBS Letters. 409: 53-56). However, Pupo et al (2002) later conclude, "nNOS does interact with full-length α1A-ARs, but that this interaction is not subtype-specific and does not require the C-terminal tail, raising questions about its functional significance" (see Abstract of Pupo et al, 2002. BMC Pharmacology. 2: 17-23; cited on the 10/11/05 IDS). Importantly, Pupo teaches, "[s]tudies on α1A-ARs in transfected PC12 cells showed no role for nitric oxide in mitogenic signaling, also raising questions about the functional significance of this interaction" (pg 6).

In summary, the instant application has failed to provide guidance as to how one of skill in the art could use the claimed invention in a way that constitutes a specific or substantial utility. The proposed uses of the claimed invention are simply starting points for further research and investigation to determine which, if any, of the many PDZ protein-binding partners actually interacts with an alpha adrenergic receptor in a manner such that modulation of the interaction will result in modification of the receptor activity.

Claim Rejections - 35 USC § 112, 1st paragraph, enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4 are also rejected under 35 U.S.C. § 112, first paragraph.

Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention so that it would operate as intended without undue experimentation.

Even if the claimed invention was supported by a specific and substantial asserted utility or a well established utility, claims 1-4 would still be rejected under 35 U.S.C. 112, first paragraph.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention is a method of detecting *in vitro* binding between an "alpha adrenergic receptor C-terminal PL sequence" and a PDZ polypeptide. The specification defines a "C-terminal PL sequence" as the "amino acid sequence of the C-terminus of a PL protein (e.g., the C-terminal 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 14, 16, 20 or 25 residues)" (pg 7). This definition does not exclude internal sequences that are part of the C-terminus region of a PL protein. Furthermore, the specification does not define where the C-terminus of a protein ends and the N-terminus begins. Therefore, the term "alpha adrenergic receptor C-terminal PL sequence" has been broadly interpreted to encompass any PL sequence from an alpha adrenergic receptor.

The specification teaches the following working examples related to the claimed invention. On page 96, the specification teaches three biotinylated peptides, each of which consists of 20 amino acids selected from the C-terminal region of particular alpha adrenergic receptor: SEQ ID NO: 26 (Alpha-2A); SEQ ID NO: 27 (Alpha-2B); and SEQ ID NO: 28 (Alpha-2C). The specification describes a "G assay" in which binding to a biotinylated peptide is detected by a "colorimetric assay using avidin-HRP to bind the biotin and a peroxidase substrate" (pg 96). On pages 96-117, the specification shows the colorimetric results of assays of binding between each of a genus of PDZ proteins and either the Alpha-2A (Table 8A); Alpha-2B (Table 8B); and Alpha-2C (Table 8C). The specification concludes, "Table 8A, 8B and 8C are the first demonstrations that we have discovered of alpha 2 adrenergic receptor (A2R) interactions with PDZ domains" (pg 118).

With respect to "alpha adrenergic receptor C-terminal PL sequence", the claims encompass sequences selected from any type of A1 or A2 adrenergic receptor from any animal species; sequences of any length (as small as one amino acid in length); and sequence variants in which one or more amino acids of naturally occurring adrenergic receptor sequences are substituted, deleted, and/or inserted. As such, the claims encompass a large genus of PL sequence variants. The specification does not teach any sequences other than SEQ ID NO: 26, 27 and 28 that can bind to PDZ proteins. The specification does not teach any smaller fragments of SEQ ID NO: 26, 27 and 28 can bind to PDZ. The specification does not give guidance as to which amino acid substitutions, deletions or insertions to make to achieve any desired property, or defined a difference in structure, or difference in function, between the protein corresponding to SEQ ID NO: 26, 27 and 28 and variants of said protein.

The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's

structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. Particular regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions [see Wells (18 September 1990) "Additivity of Mutational Effects in Proteins." Biochemistry **29**(37): 8509-8517; Ngo *et al.* (2 March 1995) "The Protein Folding Problem and Tertiary Structure Prediction, Chapter 14: Computational Complexity Protein Structure Prediction, and the Levinthal Paradox" pp. 492-495]. However, Applicants have provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions.

Although the specification outlines art-recognized procedures for producing variants, this is not adequate guidance as to the nature of active variants that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, it may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. The art recognizes that function cannot be predicted from structure alone [Bork (2000) "Powers and Pitfalls in Sequence Analysis: The 70% Hurdle." Genome Research **10**:398-400; Skolnick and Fetrow (2000) "From gene to protein structure and function: novel applications of computational approaches in the genomic era." Trends in Biotech. **18**(1): 34-39; Doerks *et al.* (June 1998) "Protein annotation: detective work for function prediction." Trends in Genetics **14**(6): 248-250; Smith and Zhang (November 1997) "The challenges of genome sequence annotation or 'The devil is in the details'." Nature Biotechnology **15**:1222-1223; Brenner (April 1999) "Errors in genome annotation."

Trends in Genetics **15**(4): 132-133; Bork and Bairoch (October 1996) "Go hunting in sequence databases but watch out for the traps." Trends in Genetics **12**(10): 425-427].

Due to the large quantity of experimentation necessary to generate the large number of variants recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 112, 1st paragraph, written description

Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicants are claiming and what Applicants have possession of. Claims 1-4 are genus claims because the claims are directed to methods of screening with a genus of labeled "alpha adrenergic receptor C-terminal PL sequence" polypeptides. This genus is highly variant because a significant number of structural differences between genus members are permitted. The claims do not provide any structural limitations on an "alpha adrenergic receptor C-terminal PL sequence". The specification defines a "C-terminal PL sequence" as the "amino acid sequence of the C-terminus of a PL protein (e.g., the C-terminal 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 14, 16, 20 or 25 residues)" (pg 7). This definition does not exclude internal sequences that are part of the C-terminus region of a PL protein. Furthermore, the specification does not define where the C-terminus of a

protein ends and the N-terminus begins. Therefore, the term "alpha adrenergic receptor C-terminal PL sequence" has been broadly interpreted to encompass any PL sequence from an alpha adrenergic receptor. With respect to "alpha adrenergic receptor C-terminal PL sequence", the claims encompass sequences selected from any type of A1 or A2 adrenergic receptor from any animal species; sequences of any length (as small as one amino acid in length); and sequence variants in which one or more amino acids of naturally occurring adrenergic receptor sequences are substituted, deleted, and/or inserted. As such, the claims encompass a large genus of PL sequence variants. The specification does not teach any sequences other than SEQ ID NO: 26, 27 and 28 that can bind to PDZ proteins. The specification does not teach any smaller fragments of SEQ ID NO: 26, 27 and 28 can bind to PDZ. The specification does not give guidance as to which amino acid substitutions, deletions or insertions to make to achieve any desired property, or defined a difference in structure, or difference in function, between the protein corresponding to SEQ ID NO: 26, 27 and 28 and variants of said protein.

From the specification, it is clear that Applicants has possession of an isolated polypeptide of SEQ ID NO: 26, 27 and 28. The specification fails to describe or teach any other polypeptide which differs from the sequence of SEQ ID NO: 26, 27 and 28 and retains the characteristics of the parent polypeptide. The claims, however, are not limited to a polypeptide comprising SEQ ID NO: 26, 27 or 28.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. In the instant case, the specification fails to provide sufficient descriptive information, such as definitive structural or functional features, or critical conserved regions, of the genus of polypeptides. There is not even identification of any particular portion of the structure that must be conserved. Structural features that could distinguish encoded polypeptides in the genus from others in the protein class are

missing from the disclosure. The specification and claims do not provide any description of what changes should be made. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polynucleotides and polypeptides encompassed. Thus, no identifying characteristics or properties of the instant polypeptides are provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicants were not in possession of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed" (pg 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (pg 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In Fiddes, claims directed to

mammalian FGFs were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only a method of detecting binding using an alpha-2 adrenergic receptor C-terminal PL sequence comprising SEQ ID NO: 26, 27 or 28, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (pg 1115).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 4 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Schepens et al, 1997. FEBS Letters. 409: 53-56.

Claim 1 encompasses a method of detecting PDZ polypeptide binding to an alpha adrenergic receptor, comprising (a) combining a labeled polypeptide containing an alpha adrenergic C-terminal PL sequence with a PDZ polypeptide *in vitro*, and (b) detecting binding between the PDZ polypeptide and the alpha adrenergic receptor polypeptide. The specification teaches that "a "PL sequence" refers to an amino sequence of the C-terminus of a PL protein ... or to an internal sequence known to bind a PDZ domain." The term "C-terminal" is not given a limiting definition in the specification and broadly encompasses any sequence derived from the second half of a protein. The term "containing" has been interpreted as "comprising"

Therefore, an "α adrenergic receptor C-terminal PL sequence" encompasses any polypeptide comprising a PDZ-binding sequence from the C-terminal region of a protein.

Schepens teaches that in an interaction trap assay the "carboxyterminal tail of the rat α1C-AR" (alpha1C adrenergic receptor) showed a "strong one for α1C-AR with nNOS PDZ motif (Table 3)". In the interaction trap assay the last 114 amino acids

residues of the rat α1C-AR were fused to a transcription activation domain. This fusion protein is encompassed by the phrase "labeled polypeptide".

Therefore, Schepens anticipates instant claim 1.

Claim 4 depends from claim 1 and limits the PL polypeptide to an epitope tagged protein expressed in a host cell. As described above, Schepens teaches rat α1C-AR were fused to a transcription activation domain (TAD). The TAD protein meets the definition of an epitope tag on α1C-AR protein. Furthermore, the fusion protein was expressed in yeast strain EGY48 for conducting the interaction trap assay (pg 54, column 1). Therefore, the teachings of Schepens described above also anticipate claim 4.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schepens et al (1997. FEBS Letters. 409: 53-56), as applied to claim 1 above, and further in view of Suzuki et al (1997. Oncogene. 18: 1239-1244).

Claim 2 encompasses a method of claim 1 wherein the PL polypeptide is a biotinylated peptide.

The teachings of Schepens are summarized above. Schepens does not teach a method of screening wherein the PL polypeptide is a biotinylated peptide.

Suzuki teaches a method of detecting protein interaction by "Far Western" analysis in which a cell extract is separated by electrophoresis and probed with a biotinylated peptide. Specifically, see pg 1239, "Far-Western blotting analysis of a similar p21 digest with biotin-procaspase-3 indicated that at least the 4 K p21-fragment bound procaspase 3".

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to practice to a method comprising combining an α adrenergic peptide taught by Schepens (consisting of the last 114 amino acids residues of the rat α1C-AR) that is biotinylated as taught by Suzuki with an nNOS PDZ polypeptide as taught by Schepens on a Far Western-type blot as taught by Suzuki, and detecting binding between the same. The person of ordinary skill in the art would be motivated to use the method of detecting binding as taught by Suzuki in order to confirm the protein-protein interaction observed by Schepens in the two-hybrid assay.

Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schepens et al (1997. FEBS Letters. 409: 53-56), as applied to claim 1 above, and further in view of Mathis et al (1995. Clin Chem. 41(9): 1391-1397).

Claim 3 encompasses a method of claim 1 wherein the PL polypeptide is a fluorescence labeled peptide.

The teachings of Schepens are summarized above. Schepens does not teach a method of screening wherein the PL polypeptide is a fluorescence labeled peptide.

Mathis teaches a method of detecting protein interaction by nonradiative fluorescent energy transfer "between Eu3+ (donor) and a second fluorescent label (acceptor)" (pg 1392). Mathis teaches that these techniques will measure protein-protein interactions (see Abstract).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to practice to a method comprising combining an α adrenergic peptide taught by Schepens (consisting of the last 114 amino acids residues of the rat α1C-AR) that is labeled with a fluorescent label acceptor with an nNOS PDZ polypeptide that is labeled with an Eu3+ donor, and detecting binding between the same by measuring fluorescent energy transfer. The person of ordinary skill in the art would be motivated to use the method of detecting binding as taught by Mathis in order to confirm the protein-protein interaction observed by Schepens in the two-hybrid assay.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachary C. Howard whose telephone number is 571-272-2877. The examiner can normally be reached on M-F 9:30 AM - 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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/Elizabeth C. Kemmerer/
Primary Examiner, Art Unit 1646